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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,614	05/08/2001	Yashwant M. Deo	MXI-166	4957

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LAHIVE & COCKFIELD, LLP.
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/851,614	DEO ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *79-93* is/are pending in the application.

4a) Of the above claim(s) *92 and 93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *79-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 79-93 are pending.

2. Claims 92 and 93 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 79-91 are being acted upon.

3. Applicant's amendments, remarks, filed 5/03/05, are acknowledged. All previous claims have been canceled. Accordingly, all previous rejections have been withdrawn. As appropriate, Applicant's remarks regarding a previous rejection will be addressed. Note that because the complete V_L and V_H sequences of antibody B11 are disclosed, the previous rejection under the first paragraph of 35 U.S.C. 112 of the claims regarding the need for an antibody deposit has been withdrawn.

4. The following are new grounds of rejection necessitated by Applicant's amendment.

5 The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6 Claim 81 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically:

A) In Claim 81, human germline V_H 5-51 gene and human germline V_k L15 gene comprise vague and indefinite terms - in the given context they appear to comprise undefined laboratory designations.

In response to a previous rejection, Applicant argues that the terms were well-known in the art at the time of the rejection as those used by Kabat et al. (1991). Applicant argues that newly submitted Tomlinson et al. and Cox et al. demonstrate the routine usage of germline nomenclature.

Applicant is advised that the there is no disclosure that V_H 5-51 and V_k L15 are the terms of Kabat et al.; neither Tomlinson et al. and Cox et al. appear to teach either term.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 79-91 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of:

A) An isolated human monoclonal antibody, or an antigen-binding portion thereof, comprising CDR1, CDR2, and CDR3, amino acids 31-35, 50-66, 99-105 of SEQ ID NO:4, respectively, and CDR1, CDR2, and CDR3, amino acids 24-34, 50-56, 99-97 of SEQ ID NO:2, respectively (Claim 79).

B) An isolated human monoclonal antibody, or an antigen-binding portion thereof, which binds to human DCs, comprising antibodies comprising portions of the V_L and V_H regions of SEQ ID NOS:2 and 4, respectively (Claim 80).

C) An isolated human monoclonal antibody, or an antigen-binding portion thereof, comprising ... V_H 5-51 and V_k L15 (Claim 81).

D) an antibody … internalized following binding to the cells (Claim 82).

E) an antibody … with an affinity of at least about 10^8 M^{-1} (Claim 83).

F) an antibody … which activates human DCs (Claim 84).

G) an antibody … when linked to an antigen, enhances presentation of the antigen by human DCs … (Claim 85).

H) an antibody … which induces cytokine release (Claim 86).

I) an antibody … which binds SEQ ID NO:7 (Claim 87).

J) an antibody … which dissociates from DCs with a rate of $10^{-3}S^{-1}$ or less (Claim 88).

K) an antibody … which comprises a kappa light chain (Claim 90).

Applicant's amendment, filed 5/03/05, asserts that support for the new limitations can be found at various sites. Note that Applicant's citing support in Claims that are not original claims, i.e., Claims 56 and higher, cannot support the invention as now claimed. Support must be found in the specification and claims as filed. As set forth below, support for the aforementioned specific limitations has not been found.

Regarding A), Applicant cites page 10.

Page 10 does no disclose these specific CDRs found in the B11 antibody. Note: Applicant has argued in response to a previous rejection that the CDRs constitute a recognizable portion of a variable region. Applicant is advised that whether the CDRs are recognizable or not is not the question. It is the Examiner's position that the specification does not adequately describe antibodies comprising the claimed CDRs in other framework regions.

Regarding B), Applicant cites Figure 13.

Figure 13 discloses only the V_L and V_H regions of SEQ ID NOS:2 and 4, it dose not disclose entire antibodies comprising these regions. Note: Applicant has argued in response to a previous rejection that the specification and prior art would have allowed for the production of antibodies comprising these variable regions. Applicant is advised that such an argument would be appropriate for a rejection for lack of enablement; the instant rejection is for inadequate written description.

Regarding C), Applicant cites page 12.

Page 12 does no disclose these antibody germline genes. Note: Applicant has argued in response to a previous rejection that the germline regions of the claims were well-known in the art at the time of the invention. Applicant is advised that well-known or not, the germline regions of the claims are not disclosed in the specification.

Regarding D) E), F), G), H), J) Applicant cites page 3.

Page 3 does not recite these limitations in the context of the B11 antibody of SEQ ID NOS:2 and 4. Additionally, no affinity of at least about 10^8 M^{-1} is disclosed and there is no disclosure of an antibody which dissociates from DCs with a rate of $10^{-3}S^{-1}$ or less.

Regarding I), Applicant cites page 64.

Page 64 discloses this limitation only for the B11 antibody, not the antibody of Claims 79 or 81, i.e., an antibody with a specific V light and V heavy portion but any constant portions.

Regarding K), Applicant cites original Claim 12 and page 2.

The specification discloses only an IgG1kappa light chain.

9. Claims 81-91 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Under *Vas-Cath, Inc. v. Mahurkar* , 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention, and that the invention, in that context, is whatever is now claimed.

There is insufficient written description to show that Applicant was in possession of:

An isolated human monoclonal antibody comprising the product of the human germline V_H 5-51 gene and human germline V_k L15 gene.

The germline genes of the claim are not disclosed in the specification. It is unclear how the specification could be considered to adequately describe any invention which is not actually disclosed in said specification. Regardless, one of skill in the art would conclude that the specification fails to disclose a representative number of species, e.g., none, to

describe the claimed genus of antibodies comprising the variable regions encoded by V_H 5-51 and V_k L15 and any constant regions. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

10. Claims 79-91 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Regarding novel methods involving biological processes, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)". The MPEP further states that physiological activity can be considered inherently unpredictable.

With these teachings, establishing the unpredictability of the art in mind, the instant specification would require a significant disclosure to enable the antibodies of the instant claims. In particular, the specification must show that an

antibody defined only by the 6 CDR's of SEQ ID NOS:2 and 4 would function for its intended use.

In addition to CDRs, antibodies comprise variable framework regions as well as constant regions. For the antibodies of the claims to function, i.e., minimally, to bind their disclosed antigen, the antibody's CDR's would have to play an exclusive role in antigen binding. While CDR's play a major role in antigen binding, it is well-established that they do not play an exclusive role in said binding. See for example, Potter et al. (2002) wherein the authors teach that amino acid residues within the framework region of an antibody can be critical for antigen binding (see particularly, Figure 2). Chien et al. (1989) teaches that even amino acids outside the framework region can be critical for antigen binding (see particularly, Figure 2). And Tempest et al. (1994) teaches that even when antigen binding and affinity are maintained, minor substitutions in the framework region of an antibody can grossly affect antibody *activity* (see particularly, Table 2 and Figure 2). Thus, the notion that all that is required to define an antibody are 6 CDR regions is firmly dispelled by the antibody engineering art.

Given that the instant specification provides no examples of the antibodies of the instant claims, other than B11, and given the fact that the specification does not even discuss any of the parameters and potential pitfalls of antibody engineering, one of ordinary skill in the art must conclude that the specification fails to adequately disclose how to make and use the claimed invention. Thus, the invention is considered to be highly unpredictable and requiring of undue experimentation to practice as claimed.

11. No claim is allowed.

12. Applicant indicates that the references from the prior IDS's that were not previously received have been enclosed as Appendix J. No Appendix J has been received.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

15. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

7/15/05

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600